REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining be allowed.

Claim Amendments

Claim 9 has been amended to recite an isolated cell.

Claims 9 and 14 have been amended to recite an methionine aminopeptidase, for which support can be found throughout the application, for example, in [0040] (page 5). Furthermore, claims 9 and 14 have been amended to recite "wherein the methionine aminopeptidase is at least about 90% identical to SEQ ID NO:1 outside of residues 168, 206 and 233." Support for this recitation can be found, for example, in [0072] (page 13).

Claim 14 has also been amended to recite an isolated nucleic acid. Support for this recitation can be found, for example, in [0078] (pages 14-15). In accordance with this amendment, claims 15, 16 and 24-30 have also been amended to recite a nucleic acid.

Claims 18-23 have been rewritten to depend, directly or indirectly, from claim 14 in preparation for a rejoinder.

New claims 35 and 36 have been added. These claims depend from claims 9 and 14, respectively, further reciting a 95% identity. Support for the recitation of a 95% identity can be found, for example, in [0072] (page 13).

No new matter has been added by these amendments. The Examiner is hereby requested to enter these amendments.

Applicants submit that all claim amendments presented herein or previously are made solely in the interest of expediting allowance of the claims and should not be interpreted as acquiescence

to any rejections or ground of unpatentability. Applicants reserve the right to file at least one continuing application to pursue any subject matter that is canceled or removed from prosecution due to the amendments.

Rejections Under 35 U.S.C. §101

The rejection of claims 9-13 under 35 U.S.C. §101 for allegedly being directed to non-statutory subject matter has been obviated for the reasons set forth below.

Previously presented claim 9 is directed to a cell comprising a polypeptide that comprises an engineered version of SEQ ID NO:1, wherein residue 206 or 233 of SEQ ID NO:1 is substituted with an amino acid selected from the group consisting of Gly, Thr, Asp, Val and Asn. The Office Action states that this claim allegedly fails to distinguish a cell that is present in nature in its native state, on the ground that the "engineering" may occur due to random mutation in a chromosomal DNA sequence. Applicant does not agree. However, in the interest of expediting prosecution, claim 9 has been amended to recite "an isolated cell" as suggested by the Office Action. Thus, the rejection has been overcome, and its withdrawal is respectfully requested.

Rejections Under 35 U.S.C. §112, Written Description

The rejection of claims 9-16 and 24-34 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, is respectfully traversed for the reasons set forth below.

As amended, claim 9 is directed to an isolated cell comprising a methionine aminopeptidase that comprises an engineered version of SEQ ID NO:1, wherein residue 206 or 233 of SEQ ID NO:1 is substituted with an amino acid selected from the group consisting of Gly, Thr, Asp, Val and Asn, and wherein the methionine aminopeptidase is at least about 90% identical to SEQ ID NO:1 outside of residues 168, 206 and 233.

The written description requirement for a claimed genus can be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, Paragraph 1, "Written Description" Requirement, Federal Register 66(4):1099, 1106 (2001).

For instance, in Example 14 (page 53-55) of the Written Description Training Materials, the claim of interest is directed to a protein having a specific sequence, and variants thereof that are at least 95% identical to the specific sequence and catalyze the reaction of A -> B. The specific sequence is novel; the specification contemplates but does not exemplify any variant of the protein. Although only one species is disclosed (the specific sequence without any deletion, insertion or substitution), this claim is deemed adequate in written description because the specification discloses the specific sequence and an assay for the A -> B reaction. The Training Materials reason that the single disclosed species is representative of the genus because all members have at least 95% structural identity with the reference compound, and because of the presence of an assay for identifying all of the at least 95% identical variants of the specific sequence which are capable of the specified catalytic activity.

The present application provides far more identifying characteristics than Example 14 of the Training Materials, thus it supports a larger genus. In addition to a specific sequence (SEQ ID NO:1) and an assay (methionine aminopeptidation), numerous variants and their activities are disclosed (see, *e.g.*, [0071] and Examples 2-8 of the present application). Furthermore, there is vast knowledge in the art about this enzyme's structure-function relationship. Exemplary publications include (all previously submitted in an IDS):

- Lowther, W. T., et al. (1999) Escherichia coli methionine aminopeptidase: implications of crystallographic analyses of the native, mutant, and inhibited enzymes for the mechanism of catalysis. *Biochemistry* 38:7678-7688. This publication discloses the

crystallographic structure of the *E. coli* methionine aminopeptidase and the importance of a number of amino acid residues in the structure.

- Lowther, W. T., and Matthews, B. W. (2000) Structure and function of the methionine aminopeptidases. *Biochim. Biophys. Acta.* 1477:157-167. This publication reviews the structure-function relationship of methionine aminopeptidases.
- Chiu, C. H., et al. (1999) Amino acid residues involved in the functional integrity of Escherichia coli methionine aminopeptidase. *J Bacteriol* 181:4686-4689. This reference studies the effects of certain mutations in the metal-binding and putative substrate binding sites of the *E. coli* methionine aminopeptidase.

In view of the disclosed and known knowledge, the present application discloses representative species of a genus commensurate with the scope of the claims, and written description is adequate for the claimed genus.

Accordingly, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §112, Enablement

The rejection of claims 9-16 and 22-34 under 35 U.S.C. §112, first paragraph, as allegedly not being enabled, is respectfully traversed for the reasons set forth below.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. MPEP §2164.01; *United States v. Telectronics, Inc.*, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988).

A representative claim of this application is directed to an isolated cell comprising a methionine aminopeptidase that comprises an engineered version of SEQ ID NO:1, wherein residue 206 or 233 of SEQ ID NO:1 is substituted with an amino acid selected from the group consisting of Gly, Thr, Asp, Val and Asn, and wherein the methionine aminopeptidase is at least about 90% identical to SEQ ID NO:1 outside of residues 168, 206 and 233. One reasonably skilled in the

art would have been able to make and use the invention from the disclosures in the application coupled with information known in the art, without undue experimentation. As discussed above, the present application, as well as publications available at the time this application was filed, provides ample information about the structure and function of methionine aminopeptidases. Methods of constructing mutants of a given polypeptide are well known in the art, and methods of testing methionine aminopeptidase activities are both disclosed herein and known in the art. Therefore, it is well within the skill in the art to identify potential amino acids that may be mutated without destroying the methionine aminopeptidase activity, and to test the activities of the resulting mutants.

A considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 8 USPQ 2d 1401, 1404 (Fed. Cir. 1988). In the present case, the scope of the claims is reasonable (90% identical to a relatively small polypeptide), the structure-function relationship of the sequence at issue is well-documented and/or disclosed, and the skill in the art is high. Therefore, no undue experimentation would be necessary.

Accordingly, withdrawal of this rejection is respectfully requested.

Conclusions

For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's objections and rejections are hereby requested. Allowance of the claims remaining in this application is earnestly solicited.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at (650) 839-5044.

Enclosed is a $50.00 check for the excess claim fees. Please apply any other charges or credits to deposit account no. 06-1050.

Respectfully submitted,

Date: March 21, 2006

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